Appendix M
Echo-Doppler Protocol

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The use of prosthetic valves over the last three decades represents a major advance in the therapy of valvular heart disease, but requires that the condition of the valve be evaluated periodically. Cardiac catheterization has been a reliable diagnostic tool in the evaluation of prosthetic valve performance. However, being an invasive technique, it cannot be performed repeatedly and involves some degree of risk. With conventional 2-D and M-Mode echocardiography and the more recent advent of color Doppler echocardiography it is now possible to have a comprehensive and accurate non-invasive hemodynamic evaluation of valve function.

I. DOPPLER ECHOCARDIOGRAPHY PROCEDURES

This section outlines the standard transducer positions, viewing planes and parameters collected using 2D/M-Mode, pulsed wave (PW), continuous wave (CW) and color flow imaging for prostheses in the aortic position and for prostheses in the mitral position.

A formal succession of standard regions of interrogation should be used during a Doppler echocardiographic examination. Using the transthoracic approach, a step-by-step protocol should include the left parasternal, apical and periapical, right parasternal, subcostal and suprasternal standard transducer positions. Because prosthetic valves generate complex flow patterns that need to be investigated in three dimensions, use of unusual windows and multiple planes (standard and non-standard) of interrogation is usually necessary to optimize the correct acquisition of chocardiographic data parameters.

If clinically indicated, the examination can be performed using the transesophageal echocardiographic approach. Transesophageal echocardiography (TEE) can provide higher quality imaging and give important information on cardiac morphology and function beyond that available from the transthoracic approach, particularly for mitral valves. Biplane TEE allowing both transverse and longitudinal plane imaging enables a more complete examination than is possible with conventional single plane TEE. New transducer technology with capability of anteroflexion, retroflexion, side-to-side movement and rotation permits additional arbitrary imaging planes to be obtained thus enabling the examiner to visualize the three-dimensional heart using two-dimensional technology and many tomographic sections. As with transthoracic echocardiography, TEE should be performed in a comprehensive and systematic fashion including the standard transgastric, esophagogastric and mid-esophageal imaging views.

For each window/transducer position, the echocardiographic examination should include 2D and M-Mode recording for obtaining structure, function and timing information. Then, after adequate gain setting and adjustement, color Doppler should be used to assess flow patterns and to guide pulsed and continuous Doppler measurements. Because the flow characteristics of prostheses vary with each valve design and geometry, the examination should be optimized by knowing the in-vitro velocity and flow patterns specific to the study valve as determined by the pre-clinical testing. When

technically possible, pulsed Doppler (PW) measurements should be attempted distal to the prosthetic valve. This is intended to spatially locate the maximum velocity region and should compare with the maximum value obtained with continuous Doppler (CW). Great care must be taken to ensure a minimum angle between the Doppler beam and the jet (as close to 0° as possible and always < 20°). Since jets vary in length and direction, the examiner must not be lulled into security by positioning the cursor symmetrically with respect to the valve ring, the chamber or vessel walls. Angle correction or automatic adjustment of the ultrasound beam for the best angle to blood flow are features available on modern Doppler equipments. However, because angle correction can amplify errors in certain situations, it is preferable to maximize the recorded velocity by using multiple windows and/or color Doppler information.

A. Prosthetic Valve in Aortic Position

A1. Approaches and viewing planes

Transthoracic approach:

Conventional 2D/M-Mode and color Doppler examinations can be performed using the following standard views: the parasternal long and short axis, the apical long axis and five chamber, the high right parasternal long and short axis, the suprasternal long and short axis.
The PW and CW Doppler examinations are best accomplished from the apex and from the suprasternal notch or the right upper sternal border. The last two approaches are usually very useful for assessing the flow through and downstream from the valve in situations of masking by the prosthesis. Occasionally, the subcostal regions can help in optimizing the ultrasonic signals.
Color Doppler assessment of the origin of a regurgitant jet is conducted using the parasternal long and short axis views whereas the total extent of regurgitant flow is best estimated using the apical window, and sometimes the subcostal or right parasternal views.

Transesophageal approach:

The aortic prosthesis is best interrogated using the longitudinal plane, in both long and short axis, obtained at the basilar level or even slightly proximal. Typical angular orientation for multiplane imaging is approximatively 40° from the transverse plane for aortic valve short-axis imaging and 130° for the long-axis. Supplementary views are the transverse short-axis view of the valve or the apical long-axis view obtained by anteroflexion of the transducer tip after obtaining of the four chamber view.
TEE is best suited for evaluation of structural abnormalities such as vegetation, annular abcscess, and rupture of intervalvular fossa. Assessing regurgitation is best performed using the transthoracic approach.

A2. Measurements

2D/M Mode Measurements

Valve structure and function: 2D and M-Mode can detect and evaluate the importance of valve rocking; for tissue valves: abnormal cusp thickness, degree of cusp calcification, reduced cusp opening, cusp prolapse/flailing, cusp perforation; presence of panus or extraneous echoes such as those generated by thrombus or vegetation, and valve bed abnormality such as ring abscess or pseudoaneurysm. 2D measurements of the mitral or pulmonic valve annulus can be used for computation of regurgitant fractions. Color-encoded M-mode recordings can help for the determination of regurgitant jet duration.

LVOT: accurate measurement of LVOT diameter is critical for determining LVOT area itself used for calculating prosthetic valve area with the continuity equation. Therefore careful attention should be given in measuring LVOT diameter: image should be frozen at mid-systole (using cineloop if available), diameter should be measured immediately below the aortic valve at the junction of the anterior sewing ring and ventricular septum, and at the junction of the posterior sewing ring and anterior mitral leaflet, with the ultrasonic beam as perpendicular as possible to the LVOT.

Left ventricular (LV) systolic function: diastolic and systolic cavity dimensions can be used to calculate LV areas and volumes, the ejection fraction and the cardiac output.

Other 2D/M Mode assessments: these include (but are not limited to) LV diastolic and systolic wall thickness, regional wall motion, left atrial and right cavity dimensions, aortic root, non-study (non-IDE) valves structure and function (as described above for the study valve), abnormalities such as thrombus or tamponade.

Pulsed and Continuous Wave Doppler Measurements

Most of the time, PW and CW Doppler examinations of aortic prosthetic valves require using multiple transducer locations and motions until the highest possible velocity and adequate waveforms, corresponding to the the best beam-jet alignment, are detected by both auditory and spectral signals.

PW Doppler measurements of transprosthetic velocity (if not aliased) are obtained by placing the sample volume just distal to the leaflets/occluder. PW Doppler is most useful to determine the LVOT velocity. From the apical window, the sample volume is placed into the prosthetic valve leaflets and gradually moved apically until a clear spectral display is observed. This usually occurs around 0.5 cm or further upstream from the valve. Caution has to be made to avoid placing the sample volume too close to the valve, in the convergence area, where the blood is already starting to accelerate. The PW velocity curves enable calculation of the LVOT peak velocity, and by tracing the modal or single darkest contour, the LVOT time-velocity

integral (TVI). If the transprosthetic velocity is not aliased, similar calculations can be made for the aortic peak velocity and the transvalvular TVI. Transvalvular and LVOT velocities are used for pressure drop, effective orifice area and stroke volume computation.

Assessment of aortic insufficiency is possible by looking for reverse flow in the LVOT, the ascending aorta, the aortic arch and descending aorta. Pulsed Doppler determination of the flow velocity through a non-regurgitant valve (mitral or pulmonic) can be used in conjunction of the transprosthetic velocity for calculation of the respective stroke volumes and the regurgitant fraction.

CW Doppler allows measurements of the transvalvular peak velocity and transvalvular TVI, the LV ejection time, and the time-to-peak velocity. If aortic regurgitation is present, the CW spectrum may give information on the regurgitation intensity and, when possible, on jet velocity, duration and pressure half-time.

Color Flow Imaging

As in the PW and CW examinations, acquisition of good quality imaging requires multiple transducer positions and planes with multiple transducer angulations. This is usually necessary to best characterize the specific transprosthetic forward flow patterns of the study valve, to distinguish prosthetic regurgitation from spurious signals due to septum motion or mitral inflow and to minimize the effects of ultrasonic attenuation and/or reverbatory artifacts generated by the prosthesis. Color Doppler echocardiography allows direct visualization of prosthetic regurgitation which appears either as a mosaic pattern of red, blue and green or simply as reverse diastolic flows in the LVOT. The origin (valvular or perivalvular), number, direction and spatial distribution of the regurgitant jet(s) can accurately be determined in the majority of the cases from the transthoracic approach. TEE can be reserved for difficult cases or for further assessment of prosthetic valve structure or perivalvular complications. Color Doppler flow imaging also provides clues to the possibility of transprosthetic obstruction in the instance of significant jet narrowing or modification of jet display.

B. Prosthetic Valve in Mitral Position

B1. Approaches and viewing planes

Transthoracic approach:

The standard views for conventional 2D/M-Mode and color Doppler echocardiography are the parasternal long and short axis and the apical and para-apical four chamber and long axis. Sometimes additional information may be obtained using a subcostal and low/mid right parasternal approach. The CW, PW Doppler and color Doppler evaluation of forward flow are best conducted from the apex. For detection and assessment of regurgation, the

use of the last two techniques from the apical window is often ignificantly limited because regurgitant jets are masked by reverberations resulting from the prosthesis. In this case, it is best to use a parasternal window which looks behind the valve prosthesis or, if indicated, a transesophageal approach.

Transesophageal approach:

Optimal visualization of the prosthetic apparatus and leafleat opening is commonly obtained from the basilar four chamber view in the transverse plane. The left appendage and the pulmonary veins are best imaged from this mid-esophageal window , in transverse and longitudinal planes. A short axis view of the mitral orifice can be obtained by anteroflexion of the transducer from the lower esophageal or transgastric windows. In the longitudinal plane, the most commonly used views are the left ventricular inflow and the long axis views obtained at the mid-esophageal level. In both planes, scanning the entire annulus by anteroflexion, retroflexion and up-and-down movements of the transducer will help detect perivalvular lesions and eccentric regurgitation. Regurgitant jets are more difficult to assess from the transgastric planes as opposed to the supradiaphragmatic and esophageal planes.

B2. Measurements

2D/M-Mode Measurements

Valve structure and function: 2D and M-Mode can detect and evaluate the importance of valve rocking; for tissue valves: abnormal cusp thickness, degree of cusp calcification, reduced cusp opening, cusp prolapse/flailing, cusp perforation; presence of panus or extraneous echoes such as those generated by thrombus or vegetation, and valve bed abnormality such as ring abscess or pseudoaneurysm. The assessment of prosthetic insufficiency can include 2D annulus measurements of the aortic or pulmonic valve for computation of regurgitant fractions.
Other 2D/M Mode assessments include, but are not limited to, LV diastolic and systolic cavity dimensions (from which can be derived the LV areas and volumes, ejection fraction and cardiac output), diastolic and systolic wall thickness, regional wall motion, left atrial and right cavity dimensions, aortic root, non-study (non-IDE) valves structure and function (as described above for the study valve), abnormalities such as thrombus or tamponade.

Pulsed and Continuous Wave Doppler Measurements

Pulsed Doppler interrogation from the apical window is used to assess the forward transprosthetic flow. The sample volume is placed just distal to the valve leaflets or occluder and oriented until the highest possible velocity with adequate waveform is obtained. If not aliased, the PW transvalvular velocity is used to calculate the transprosthetic peak velocity and the transprosthetic TVI.
Evaluation of the forward flow within the left atrium (LA), approximatively

within 1 cm proximal to the prosthetic valve, should be attempted. This is often difficult using the transthoracic approach, due to shadowing from the prosthesis. The LA velocity can be recorded from the transesophageal approach if TEE is performed. The LA velocity profiles are used to compute the proximal term of the pressure drop equations. Pulsed Doppler interrogation in the LVOT and pulmonic can be performed for determination of regurgitant fractions.

CW Doppler interrogation is accomplished from the transthoracic apical/periapical window. The CW transvalvular velocity profiles permit evaluation of the mitral peak velocity, TVI, pressure gradients, pressure half time ($P\frac{1}{2}t$) and deceleration time.

Color Flow Imaging

Most of the time, good quality imaging of the forward transprosthetic flow is obtained from the transthoracic apical window.As opposed to the imaging of the forward flow, visualization of prosthetic regurgitation from the transthoracic window, either apical or parasternal, is usually challenging. Regurgitant jets are often masked from the apex due to shadowing by the prosthesis. Their detection may be furthermore difficult in cases of eccentric jets, thus sweeping arround the LA. Observation of a LV proximal acceleration zone may significantly help in identifying valvular regurgitation. However, it must be admitted that one cannot effectively rule out a mild to moderate prosthetic valvular leak by transthoracic echo. If there is a strong suspicion, TEE is the only reliable method to detect and differentiate mitral regurgitant jets.

	AORTIC VALVE	MITRAL VALVE
TRANSTHORACIC	2D. parasternal LA/SA . apical LA/5 chamber . right parasternal LA/SA . suprasternal supraclavicular PW, CW: best from apex or suprasternal. Color Doppler for regurgitation: . parasternal(origin) . apex (extent)	2D. parasternal LA/SA . apical LA/4 CH . subcostal . right parasternal PW, CW, color Doppler: best from apex
TRANSESOPHAGEAL	. longitudinal plane: basilar LA/SA . transverse plane: basilar SA, apical LA	. transverse plane: basilar 4 chamber/LAA OG junction SA . longitudinal plane: mid-O LV inflow/LA

APPROACHES AND MOST COMMONLY USED VIEWING PLANES

LA	Long Axis	mid-O	mid-oesophagus
SA	Short Axis	LV	left ventricular
OG	Oesophagogastric	LAA	left atrium appendage

II. ECHOCARDIOGRAPHIC PARAMETERS AND CALCULATION METHODS

A complete echocardiographic study should provide the following data parameters: stroke volume and cardiac output, peak pressure gradient, mean pressure gradient, effective prosthetic valve area, prosthetic valve regurgitation assessment. For patients in sinus rhythm, an average of at least three cardiac cycles should be used to determine the measurements from which are derived the data parameters. For patients with rhythm disturbance, an average of at least five cycles should be used.

A. Cardiac Output

Evaluation of cardiac output (*CO*) can be obtained using either Doppler or 2D echocardiography. *CO* (in l/min) corresponds to the product of the stroke volume (*SV*) by the heart rate (*HR*):

$$CO = SV \times HR$$

The Doppler method for obtaining the left ventricular *SV* utilizes the following equation:

$$SV = TVI \times CSA$$

where *TVI* = systolic velocity time interval of the LVOT or
= $V_{mean\ LVOT}$ X ejection time,
CSA = cross sectional area of the LVOT or aortic root.

2D methods permit estimation of the LV end-diastolic volume (*EDV*), the LV end-systolic volume (*ESV*) and stroke volume (*SV*) as follow:

$$SV = EDV - ESV$$

LV volumes are calculated using either the following biplane or single plane algorithms, based on apical imaging from either the four-chamber and/or the two-chamber views, assuming axial or elliptical symmetry:

1. Biplane method of discs summation (modified Simpson's rule)

Calculation of volumes results from summation of areas from orthogonal diameters of n cylinders of equal height (by dividing left ventricular longest length into n equal sections):

$$V = \frac{\Pi}{4} \sum_{i=1}^{n} a_i \, b_i \cdot \frac{L}{n}$$

where V = LV volume (endsystolic or enddiastolic), in cm^3
a_i and b_i = diameters from the two orthogonal planes, in cm
L = length of left ventricule, in cm
n = number of slices

There are no data about the ideal number of dics/slices. Although 20 slices are commonly employed, a minimum number of 4 can be accepted. These calculations are eased by computer programs of modern echocardiographic equipments and by new accoustic quantification approaches which derive LV volumes on-line from automated border detection based on backscatter analysis.

2. Single plane area length method

This method was developed for angiography and is applicable only if the Doppler method and/or the disc summation method are not obtainable.

$$V = 0.85 \, \frac{(A)^2}{L}$$

where A = area of left ventricular cavity, in cm^2
L = length of left ventricular cavity, in cm.

B. Peak Pressure Gradient

The peak velocities obtained by CW Doppler and PW Doppler are converted into pressure gradients by applying the Bernoulli equation:

$$\Delta P_{peak} = 4 (V_2^2 - V_1^2)$$

where ΔP_{peak} = peak systolic (for aortic valve) or diastolic (for mitral valve) pressure gradient in mm Hg,
V_2 = prosthetic orifice peak velocity as measured by CW, in m/sec
V_1 = peak velocity proximal to the valve, as measured by PW from the LVOT for aortic valves, in m/sec, or from the LA for mitral valves, in m/sec.

Unless PW measurement of the proximal velocity term is unavailable, the simplified version of the Bernoulli equation, where the proximal velocity

term V_1 is dropped, should not be used for calculation of the prosthetic eak pressure gradient.

C. Mean Pressure Gradient

Whenever possible the mean pressure gradient is calculated using the ultrasound instrument measurement package. Most software packages of modern ultrasound systems allow planimetry of the Doppler spectral envelope and calculation of the mean pressure gradient by averaging the instantaneous pressure gradients over the relevant flow period duration. The mean transvalvular pressure gradient is obtained by subtracting the proximal mean pressure from the distal mean pressure:

$$\Delta P_{mean} = P_2 - P_1 \quad Method(1)$$

where ΔP_{mean} = mean pressure gradient in mm Hg,
P_2 = prosthetic mean pressure as estimated from CW, and
P_1 = proximal mean pressure measured by PW from the LVOT for the aortic prosthesis, or from the LA for the mitral prosthesis.

When not provided by the computer software package of the ultrasound machine, the mean pressure gradient can be estimated indirectly from the ⁻oppler spectra. This implies estimating V_{rms} (square root of the mean of ₋he square of the velocity):

$$V_{rms} \simeq C \; X \; Vpeak$$

Where C = 0.73 for parabolic shaped velocity curve
= 0.58 for triangular shaped velocity curve

Then

$$\Delta P_{mean} = 4\left[(V_{rmsd})^2 - (V_{rmsp})^2\right] \quad Method(2)$$

where ΔP_{mean} = mean pressure gradient in mm Hg,
V_{rmsd} = root mean square velocity distal to the valve in m/sec, and
V_{rmsp} = root mean square velocity proximal to the valve in m/sec.

It should be recognized that *Method(2)* is very subjective and prone to errors because it requires interpretation of the shape of the waveform. Therefore Method(1) should be preferred.

D. Effective Orifice Area

D 1. Prosthetic Valve in Aortic Position

The Effective orifice area (EOA) is equal to flow rate divided by velocity. EOA can be calculated by applying the continuity equation which is based on the principle that, in the absence of shunt or significant valvular regurgitation, the volume of blood passing proximal and distal to a cardiac valve is the same. This equivalence between proximal and distal volumetric flows can be expressed as:

$$Prosthetic\ Aortic\ EOA\ X\ TVI_{AO} = CSA_{LVOT}\ X\ TVI_{LVOT}$$

where CSA_{LVOT} = cross sectional area of the LVOT using 2D measurement of the LVOT diameter ($\pi D^2 / 4$), in cm^2,

TVI_{LVOT} = velocity time integral over forward flow derived from the PW Doppler spectrum obtained in the LVOT, in cm,

TVI_{AO} = velocity time integral over forward flow derived from the transvalvular maximal velocity CW Doppler spectrum, in cm.

Therefore

$$Prosthetic\ Aortic\ EOA = \frac{CSA_{LVOT}\ X\ TVI_{LVOT}}{TVI_{AO}} = \frac{SV}{TVI_{AO}}$$

Where SV = stroke volume, in cm^3

TVI may be provided by equipment computer software integration of the flow profile recorded at the location of maximal velocity, or may be calculated as

$$TVI = V_{mean}\ X\ ET$$

where V_{mean} = mean velocity of the flow profile over forward flow,

ET = ejection time.

SV can be calculated using CSA_{LVOT} and TVI_{LVOT} measurements, or in any of a number of ways (using the pulmonary artery outflow or mitral annular flow, or even any cardiac output measurement).

Calculation of EOA using sewing ring area for CSA_{LVOT} can be reported in addition to the standard method using the CSA of the LVOT.

Prosthetic aortic EOA can also be computed using the simplified peak elocity method which approximates the original continuity method assuming that the shape of the waveform is the same both upstream and downstream, as

$$Prosthetic\ Aortic\ EOA = CSA_{LVOT}\ X\ \frac{V_{PkLVOT}}{V_{PkAO}}$$

where V_{PkLVOT} = peak velocity from PW in the LVOT, in m/sec, and
V_{PkAO} = transvalvular peak velocity from CW, in m/sec.

However, whenever possible, the method using the *SV* should be preferred.

D 2. Prosthetic Valve in Mitral Position

D 2 (i). Prosthetic mitral EOA can be estimated using the **pressure half time** ($P\frac{1}{2}t$) method. Pressure half time is defined as the time required for the peak pressure gradient to drop by one half of its initial value or the peak velocity (V_{peak}) to decrease by $\sqrt{2}$:

$$t\tfrac{1}{2} = t\left(\frac{P_{peak}}{2}\right) - t(P_{peak}) = t\left(\frac{V_{peak}}{\sqrt{2}}\right) - t(V_{peak})$$

This parameter is determined from the CW Doppler spectral trace of the prosthetic mitral inflow.

The prosthetic orifice area can be estimated by dividing the experimentally derived constant 220 by $P\frac{1}{2}t$

$$Prosthetic\ mitral\ EOA = \frac{220\ \ (cm^2.ms)}{P\tfrac{1}{2}t\ (ms)} \qquad Method(1)$$

This method is commonly regarded as a flow-independent measure in all clinical conditions and in all types of prostheses. However it should be kept in mind that pressure half time has been shown to be related to a number of factors in addition to orifice area, such as the pressure gradient at the start of diastole, stroke volume and left atrial or ventricular compliance. Also, it is important to know that this method is likely to be unreliable when adequate quality spectral wave forms are not obtained, and in the presence of atrial tachycardia, atrioventricular block, or severe aortic incompetence.

D 2 (ii). Because of these limitations, it is recommended to calculate the EOA using the **continuity equation** as follows:

$$Prosthetic\ mitral\ EOA\ X\ TVI_{MI} = CSA_{AO}\ X\ TVI_{AO}$$

or

$$Prosthetic\ mitral\ EOA = \frac{CSA_{AO}\ X\ TVI_{AO}}{TVI_{MI}} \quad Method(2)$$

where CSA_{AO} = aortic cross sectional area measured using 2-D imaging, = $\pi D^2/4$, where D = inner edge to inner edge diameter at the base of the cusps during midsystole, in cm,
TVI_{AO} = velocity time integral derived from the transvalvular aortic CW Doppler spectrum, in cm, and
TVI_{MI} = velocity time integral derived from the transvalvular mitral CW Doppler spectrum, in cm.

If a significant aortic regurgitation is present, it is best to use the following formula:

$$Prosthetic\ mitral\ EOA = \frac{CSA_{PA}\ X\ TVI_{PA}}{TVI_{MI}} \quad Method(3)$$

where CSA_{PA} = pulmonic annulus cross sectional area measured using 2D, = $\pi D^2/4$ where D = inner edge to inner edge diameter at the base of the cusps during midsystole, in cm,
TVI_{PA} = velocity time integral derived from the transvalvular pulmonic CW or PW Doppler spectrum, in cm.

E. Valve Regurgitation Assessment

Color flow Doppler, by allowing real-time beat-to-beat visualization of regurgitant jets, is of great value for detecting the presence of valvular regurgitation. However, it should be kept in mind that the extent of regurgitation, or jet size, is influenced by other factors than the regurgitation severity (regurgitant flow). These factors include jet velocity (itself dependent upon pressure gradient and systemic blood pressure), jet eccentricity, wall impingement and instrument setting. Because of this, grading of the severity of regurgitation cannot be solely based on the color flow imaging of the regurgitant jet. Since currently no

one method can accurately quantify valvular regurgitation, a comprehensive valuation is necessary that requires compilation of numerous assessments using PW, CW, color Doppler and, if indicated, a transesophageal approach. It is hoped that more accurate methods for quantifying valvular regurgitation, some being under development, will be validated and overcome the limitations of those available today.

E 1. Prosthetic Aortic Insufficiency

Information as to severity of regurgitation can be obtained in the majority of the cases with a transthoracic study. An integrated approach for qualitative and semi-quantitative assessment includes the following methods from which at least three must be concordant:

(a). **Color Doppler** criteria:
- categorization into central valvular, paravalvular or both
- grading using area and height of regurgitant jet normalizeded to area and height of LVOT respectively:

Severity	Area of jet to area of LVOT %	Height of jet to height of LVOT %
Trivial	< 4	1 - 24
Mild	4 - 24	25 - 45
Moderate	25 - 59	46 - 64
Severe	> 60	> 65

Caution: these two methods have never been validated in prosthetic valves. They can be significantly limited and misleading in very eccentric jets. Furthermore, in irregular regurgitant orifices (which may be present in many prosthetic valves) these methods have been shown to be quite unreliable, especially the simple measurement of jet height.

(b). Degree of **flow reversal** in the descending aorta by PW Doppler

(c). **Regurgitant fraction**, calculated as follows (valid if there is none or little pulmonary regurgitation):

$$\frac{SV_{AO} - SV_{PA}}{SV_{AO}} \times 100\%$$

where SV_{AO} = aortic stroke volume (Doppler), in cm^3, and
SV_{PA} = pulmonic stroke volume (Doppler), in cm^3.

See section A for *SV* calculation.

(d). **Pressure half-time** of the regurgitant jet derived from CW Doppler. Like for the mitral prosthetic half-time, it must be kept in mind that this parameter is significantly affected by nonvalvular factors such as chamber compliance and driving pressure.

E 2. Prosthetic Mitral Insufficiency

Transthoracic clues to the suspicion of significant mitral regurgitation are :

- Signals of increased mitral inflow volumes (peak early velocity > 2m/s, pressure half time < 120 ms and TVI of mitral inflow > 50 cm), combined with signs of decreased systemic output despite normal LV function.
- aliased velocity present in the zone proximal to the regurgitant orifice
- Unexplained pulmonary hypertension

Transthoracic and/or TEE color Doppler flow imaging allows the categorization of regurgitation into central, paravalvular or both.

As to the semi-quantitation of the severity of regurgitation, an integrative approach with at least three concordant findings should be used:

(a). **Color Doppler** criteria
From three transthoracic orthogonal planes, the regurgitant jet area is related to the left atrial area. The prosthetic regurgitant jet area is determined in the echo plane in which the jet area is the largest. Grading then is as follows:

Severity	Regurgitant Jet Area to Left Atrial Area %
Mild	< 20
Moderate	20 - 40
Severe	> 40

aution:
1. This method is very limited in cases of eccentric regurgitant jets. The distorting effect is such that eccentrically directed mitral jets may have an observed area of only 40% of the size of a centrally direct jet with the same regurgitant flow rate. Therefore, in situation of significant eccentricity, the regurgitant jet area should not be regarded as a factor in the assessment of severity of regurgitation.

2. From the transthoracic approach, the PW and color Doppler assessment of regurgitant jet(s) into the left atrium is often useless and/or misleading due to masking of the regurgitant jet by the prosthesis. Because of this, the threshold for performing a transesophageal echo to determine the presence and severity of regurgitation should be low.

Due to an increased sensitivity with TEE, criteria used for grading severity of regurgitation from the transesophageal approach are different. For native valves, the maximum regurgitant jet area (the greater of two or more measurements) has been associated with mild, moderate and severe mitral regurgitation when values were measured between 1.5 and 4 cm^2, between 4 and 7 cm^2 and above 7 cm^2 respectively. This method remains to be validated for prosthetic heart valves. The limitation concerning eccentrically directed jets applies for transesophageal color Doppler imaging.

(b). Pattern of **pulmonary vein flow**
Pulmonary venous flow can be recorded by PW Doppler, and systolic flow reversal (representing more than 25% of forward flow velocity) may be consistent with severe mitral regurgitation. To be noted that a moderate regurgitation associated with a jet directed toward a pulmonary orifice may also produce reversal. TEE can help in discriminating causes of flow reversal.

(c). **Regurgitant fraction**
(valid if there is little or no aortic regurgitation)

$$RF = \frac{LVSV - SV_{AO}}{LVSV} \; X \; 100\%$$

where $LVSV$ = left ventricular stroke volume, in cm^3 (2D method)
SV_{AO} = aortic stroke volume, in cm^3 (Doppler)

Calculation: see section A.

(d). **CW Doppler** recording of the regurgitant jet and its pattern
A barely identifiable CW Doppler trace generally indicates a small amount of regurgitation, particularly if the signal covers only part of the systole. A dense and early peaking of the CW Doppler regurgitation signal should be considered as an indication to pursue further assessment.

(e). Characterization of **proximal convergent flow**
he zone proximal to the regurgitant orifice must be carefully interrogated and the color velocity baseline shifted so to highlight an aliasing contour at around 20 or 30 cm/sec. The distance is measured from this contour to the regurgitant orifice and instantaneous flow rate is calculated assuming a hemispheric shape to the isovelocity:

$$Q_R = 2\ \pi\ r^2\ V$$

Where Q_R = regurgitant flow rate, in cm^3/sec or ml/sec,
r = distance from the aliased contour to the regurgitant orifice, in cm,
V = aliasing velocity, in cm/sec.

Then the regurgitant volume (RV) is calculated as follows:

$$RV = Q_R \cdot \frac{TVI_R}{V_{Rpeak}}$$

Where RV = regurgitant volume, in ml,
TVI_R = velocity time integral over the backward flow through regurgitant orifice, derived from CW, in cm,
V_{Rpeak} = peak velocity over backward flow through regurgitant orifice, derived from CW, in cm/sec.

This method presents the advantage of being quantitative. However, it has not been validated in prosthetic regurgitation.

CO	. Doppler . 2D: disc summation method (biplane) area length method (single plane)	
ΔP_{peak}	. Bernoulli equation . simplified Bernoulli equation (if proximal velocity non available)	
ΔP_{mean}	. planimetry (instantaneous pressure gradients) . V_{rms} calculated from V_{peak}	
E.O.A.	Aortic Valve: . continuity equation using *SV* . continuity equation using ratio V_{peak}	Mitral Valve: . continuity equation using *AO* and *MI*, or *PA* and *MI* flows . pressure half time
Regurgitation	. color Doppler . *AO* flow reversal . *RF* . pressure half time of regurgitant jet	. color Doppler . pulmonary vein flow . *RF* . proximal convergent flow . CW Doppler

ECHO DOPPLER PARAMETERS FOR PROSTHETIC VALVES

CO	cardiac output	ΔP	pressure gradient	RF	regurgitant fraction
SV	stroke volume	E.O.A.	effective orifice area		
V	velocity	AO	aortic	MI	mitral

F. Non-study Valve Parameters

When present, important abnormalities of cardiac structure and function should be documented in the individual report form. Such information would include for example data on non-study valve (native or other prosthetic) regurgitation (grading) and stenosis (pressure gradients, EOA) with specification of the method used, data on LV structure (e.g. LV aneurysm, significant LV hypertrophy) or function abnormalities (e.g. low ejection fraction, significant wall motion abnormalities), data on significant cavity dilatation, on apical and/or left atrial thrombi, on pericardial effusion (indicated as small, moderate,large or tamponade).

III. GENERAL INFORMATION AND DATA PRESENTATION

A. General Information

The recommended patient procedures (section I) and echocardiographic parameters and calculation methods (section II) have been developed to provide a uniform method whereby data will be common to all echocardiography centers allowing their pooling and interpretation.

Echocardiographic examination of patients is required when the patient is stable during the early post-operative follow-up (prior to discharge or within 30 days), and at the first annual follow-up.

It is recommended that an echocardiologist with knowledge of the in-vitro flow visualization testing results should be present to monitor the examination in order to ensure that all necessary views and data have been obtained with sufficient accuracy.

As echocardiographic instrumentation make and model may vary from one center to another, a description of the Doppler echocardiographic equipment for each institution should be provided (model and serial number, transducers). Also each institution is required to ensure and provide documentation pertaining to validation and calibration of each echocardiographic device used for the examinations. Validation and velocity calibration of the Doppler instruments will be in comparison with known parameters simulated by a string or a flow phantom. The minimal requirement will be a validation and calibration check within 3 months prior to the start of the clinical study and yearly thereafter.

Baseline data information should include patient I.D. number, hospital I.D. number, reason for the echo, date of implant, follow-up time (months post-op), valve size, body surface area, heart rate and dominant cardiac rythm at the time of the examination.

Each reported echocardiographic parameter should be computed by averaging three cardiac cycles if the patient is in sinus rhythm or at least five cardiac cycles if the patient presents rhythm disturbance. Care should be taken to utilize an optimal gain setting which is defined as the maximal gain level possible without introducing signals outside of flow areas or onto tissue from an adjoining chamber. All the prosthetic parameters described in section II (A, B, C, D, E) are required with specification of the method used. Regurgitation and stenosis information is also required for all remaining valves as these results may impact the prosthetic valve study. Similarly other significant non-prosthesis related abnormalities (see section II-F) should be documented and reported in the individual report forms.

Introducing a blinded assessment of the echocardiographic and Doppler parameters will enhance credibility and optimize reliability of the data collection. Analysis of both intraobserver and interobserver measurement variability within and between centers is highly recommended.

. Data Presentation

B(i). Video Tapes

Each echocardiographic examination should be recorded on standard 1/2" VHS tape. A **10% random sample** of the echocardiograms conducted should be provided and should include tapes from every participating institution. Each tape must clearly identify the tracing from which the measurements were taken. In addition, video tapes must be provided on all patients whose measurements fall out of the normal range as defined by the study investigator. Three copies of all tapes should be provided although FDA may request additional traces during the review process.

B(ii). Individual Patient Data

A listing, by patient, of the required echocardiographic data parameters at each time period will be provided as shown in table 2 for aortic valves and in table 3 for mitral valves. A 10% random sample of the collected raw data for each valve position, as shown (but not limited to, see section II-F) in table 1, should also be provided in addition to the raw data of patients with values out of the normal range as defined by the study investigator.

B(iii). Data Summary

Data will be summarized by valve size for each model (aortic and mitral) as shown in table 4 for aortic valves and table 5 for mitral valves. The tables must include N, the number of samples, standard deviation, range (maximum and minimum) for each parameter studied with the exception of regurgitation data, for which frequency distribution will be presented. Plots of distribution of pressure gradients and EOA grouped by valve size, and displaying also mean ± standard deviation of observations should be provided by time period.

TABLE 1

POSTOPERATIVE ECHOCARDIOGRAPHY: INDIVIDUAL REPORT FORM

- Patient ID _____
- Clinic ID _____
- Age _____
- Sex _____
- Date Implant _____
- Months postop _____
- Valve Size(mm) _____
- BSA(m^2) _____
- Reason for Echo _____
- Stroke Volume(ml) _____
- Heart Rate(bpm) _____
- Cardiac Output[1](L/min) _____
- Heart Rhythm _____
- Cardiac Index(L/min/m^2) _____

AORTIC VALVE

- ΔPpeak _____ mm Hg
- Vpeak LVOT _____ m/sec
- Vpeak AO _____ m/sec
- ΔPmean _____ mm Hg
- Method[2] _____
- Time Vpeak/LVET _____ %
- Time Vpeak _____ msec
- LVET _____ msec
- E.O.A.method: 1. TVI _____ cm^2
  2. SV _____ cm^2
  3. Ratio V peak _____ cm^2
- CSA_{LVOT} _____ cm^2
- Regurgitation Severity _____
  Site 1. valvular _____
  2. paravalvular _____
- Method 1. Color Doppler _____
  2. Regurgitant Fraction _____
  3. Pressure Half Time _____
  4. Aortic Flow Reversal _____

MITRAL VALVE

- ΔPpeak _____ mm Hg
- Vpeak LA _____ m/sec
- Vpeak MI _____ m/sec
- ΔPmean _____ mm Hg
- Method[2] _____
- E.O.A. _____ cm^2
- Method 1. Pressure Half Time _____ msec
  2. Continuity Equation _____
- Regurgitation Severity _____
  Site 1. valvular _____
  2. paravalvular _____
- Method 1. Color Doppler _____
  2. Regurgitant Fraction _____
  3. Pulmonary Vein Flow _____
  4. Proximal Convergent Flow _____

COMMENTS _____

_____

_____

_____

[1] Cardiac Output calculation 1. Doppler _____ 3. single plane _____
2. disc method _____ 4. other _____

[2] Method: 1. Echo machine _____
2. Vrms _____

TABLE 2

POSTOPERATIVE ECHOCARDIOGRAPHY INDIVIDUAL DATA: AORTIC VALVE

Patient ID	Clinic ID	Date (m/yr)	Months Postop	Valve Size (mm)	Heart Rate (bpm)	Heart Rhythm	CO (l/min)	CI (l/min/ m^2)	T Vpeak /LVET (%)	ΔPpeak (mm Hg)	ΔPmean (mm Hg)	E.O.A. (cm^2)	Method	Regurgitation Severity/Methods/Site	Other*

* Significant cardiac abnormality: Yes/No

TABLE 3

POSTOPERATIVE ECHOCARDIOGRAPHY INDIVIDUAL DATA: MITRAL VALVE

Patient ID	Clinic ID	Date	Months Postop (m/yr)	Valve Size	Heart Rate (mm)	Heart Rhythm (bpm)	CO (l/min)	CI (l/min /m^2)	ΔPpeak (mm Hg)	ΔPmean (mm Hg)	Pressure half time (msec)	E.O.A. (cm^2)/Method	Regurgitation Severity/Methods/Site	Other*

* significant cardiac abnormality: Yes/No

TABLE 4

SUMMARY OF ECHO-DOPPLER DATA BY VALVE SIZE: AORTIC VALVE

VARIABLE	Size 19 mm				Size 21 mm				Size 23 mm				Size 25 mm				Size 27 mm				Size 29 mm			
	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max
Months Postop																								
Heart Rate																								
CO																								
CI																								
T Vpeak/LVET																								
ΔPpeak																								
ΔPmean																								
E.O.A.																								
Regurgitation:																								
Severity 0																								
1+																								
2+																								
3+																								
4+																								
Site: central																								
paravalvular																								
both																								

TABLE 5

SUMMARY OF ECHO-DOPPLER DATA BY VALVE SIZE: MITRAL VALVE

VARIABLE	Size 23 mm				Size 25 mm				Size 27 mm				Size 29 mm				Size 31 mm				Size 33 mm			
	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max	N	Mean	S.D.	Min Max
Months Postop																								
Heart Rate																								
CO																								
CI																								
ΔPpeak																								
ΔPmean																								
E.O.A.																								
Regurgitation:																								
Severity 0																								
1+																								
2+																								
3+																								
4+																								
Site: central																								
paravalvular																								
both																								

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